

POWER OF ATTORNEY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Marton et. al.

Confirmation No.: 8604

Serial No.: 09/823,322

Art Unit: 1631

Filed: April 2, 2001

Examiner: Marschel, A.

For: METHODS FOR DETERMINING  
THERAPEUTIC INDEX FROM GENE  
EXPRESSION PROFILES

Attorney Docket No: 9301-136

**POWER OF ATTORNEY OR AUTHORIZATION OF AGENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Rosetta Inpharmatics LLC hereby revokes any and all previous powers and appoints:

Practitioners at Customer Number **20583**

as its attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith.

Please change the correspondence address for the above-identified application to:

The above mentioned Customer Number.

Practitioners at Customer Number **20583**.

Firm or Individual Name:

Address: **Jones Day**  
**222 East 41<sup>st</sup> Street**  
**New York, New York 10017**

Telephone: **(212) 326-3939**

**Statement Under 37 C.F.R. 3.73(b)**

Rosetta Inpharmatics LLC states that it is:

the assignee of the entire right, title, and interest; or  
 an assignee of less than the entire right, title and interest.  
The extent (by, percentage) of its ownership interest is %

in the patent application/patent identified above by virtue of either:

An assignment from the inventor(s) of the patent application/patent identified above.  
The assignment was recorded in the United States Patent and Trademark Office on  
at Reel , Frame , or for which a copy thereof is attached.

OR

A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as shown below:

1. From: **Matthew Marton and Roland Stughton** To: **Rosetta Inpharmatics, Inc.**

The document was recorded in the United States Patent and Trademark Office on **February 26, 1999** at Reel **9797**, Frame **0698**, or for which a copy thereof is attached.

2. From: **Rosetta Inpharmatics, Inc.** To: **Rosetta Inpharmatics, LLC**  
a copy of which is attached.

3. From: To:

The document was recorded in the United States Patent and Trademark Office on  
at Reel , Frame , or for which a copy thereof is attached.

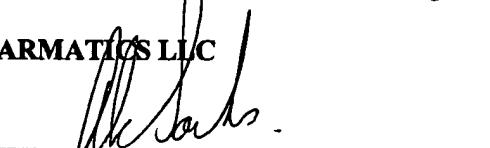
Additional documents in the chain of title are listed on a supplemental sheet.

Copies of assignments or other documents in the chain of title are attached.

[Note: A separate copy (i.e., the original assignment document or a true copy of the original document) must be submitted to Assignment Division in accordance with 37 CFR Part 3, if the assignment is to be recorded in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

**ASSIGNEE: ROSETTA INPHARMATICS LLC**

Date: 02/03/04 Signature:   
Typed Name: Alan Sachs  
Position/Title: Senior Vice President

Note: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required.

Total of \_\_\_\_\_ forms are submitted.

## ASSIGNMENT AND ASSUMPTION AGREEMENT

ASSIGNMENT AND ASSUMPTION AGREEMENT, (this "Agreement") is entered into effective as of the 1<sup>st</sup> day of December 2002, between Rosetta Inpharmatics, Inc., a Delaware corporation (the "Corporation"), and Rosetta Inpharmatics LLC, a Delaware limited liability company (the "Assignee").

### RECITALS

**A. WHEREAS**, the Board of Directors of the Corporation has decided to separate certain non-operating assets from its operating assets, retain such non-operating assets, and continue future operating assets as a limited liability company;

**B. WHEREAS**, in order to effectuate the foregoing change, the operating assets and liabilities of the Corporation must be transferred to a new limited liability company.

**C. WHEREAS**, the Corporation desires to transfer the operating assets and liabilities of the Corporation to the Assignee pursuant to the terms hereof, and the Assignee is willing to give effect to such transfer on the terms and conditions hereof.

**NOW, THEREFORE**, in consideration of the premises and of the mutual covenants and agreements set forth herein, the parties hereto hereby agree as follows:

1. **Assignment.** The Corporation hereby sells, assigns and transfers all of its right, title and interest in and to all of the assets relating to the Corporation, except as set forth on Schedule 1 (the "Assigned Assets") to the Assignee. The assets being assigned and transferred by the Corporation to the Assignee include, but are not limited to, those patents and patent applications set forth in Schedule 2.

2. **Assumption.** The Assignee accepts such Assignment of the Assigned Assets and hereby assumes all of the Corporation's obligations and liabilities relating to the Assigned Assets (the "Assumed Liabilities").

3. **Further Assurances.** The Corporation and the Assignee each agrees to take such other actions, if any, as are necessary to reflect and give effect to the transactions contemplated by this Agreement.

4. **Successors and Assigns.** This Agreement shall be binding upon, and shall inure to the benefit of, the Corporation and the Assignee and their respective successors and assigns. No person or entity shall in any respect be deemed to be a third party beneficiary with respect to this Agreement.

5. **Governing Law.** This Agreement and the rights and obligations of the parties hereto shall be interpreted, enforced in accordance with, and governed by, the laws of the State of Delaware applicable to agreements made and to be performed wholly within that jurisdiction.

6. Amendment, Waiver, etc. No amendment, modification or alteration of the terms or provisions of this Agreement shall be binding on the parties hereto unless the same shall be in writing and duly executed by such parties.

7. Headings. Section headings contained herein are for convenience of reference only and shall in no way affect the meaning or interpretation of the terms and provisions hereof.

8. Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be considered an original and all of which shall together constitute one and the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first above written.

**ROSETTA INPHARMATICS, INC.**

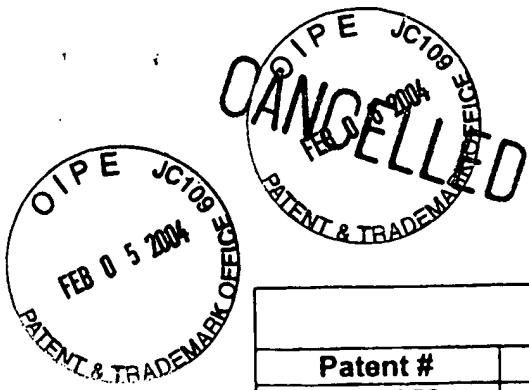
By: Caroline Dorsa  
Name: Caroline Dorsa  
Title: Vice President - Treasurer

**ROSETTA INPHARMATICS LLC**

By: Celia A. Colbert  
Name: Celia A. Colbert  
Title: Secretary

**SCHEDULE 1**

**Intercompany note in aggregate principal amount of \$10,000,000 owed by Merck & Co., Inc. to Rosetta Inpharmatics, Inc.**



SCHEDULE 2

Issued U. S. Patents

Patent #	Issue Date	Title
5,965,352	10/12/1999	Methods for Identifying Pathways of Drug Action
6,132,969	10/17/2000	Methods for Testing Biological Network Models
6,146,830	11/14/2000	Method for Determining the Presence of a Number of Primary Targets of a Drug
6,171,794	01/09/2001	Methods for Determining Cross Hybridization
6,197,517	03/06/2001	Essential Genes of Yeast as Targets for Antifungal Agents, Herbicides, Insecticides & Anti-Proliferation Drugs
6,200,803	03/13/2001	Essential Genes of Yeast as Targets for Antifungal Agents, Herbicides, Insecticides & Anti-Proliferation Drugs
6,203,987	03/20/2001	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns
6,218,122	04/17/2001	Methods of Monitoring Disease States & Therapies Using Gene Expression Profiles
6,221,597	04/24/2001	Essential Genes of Yeast as Targets for Antifungal Agents, Herbicides, Insecticides & Anti-Proliferation Drugs
6,222,093	04/24/2001	Methods for Determining Therapeutic Index from Gene Expression Profiles
6,232,068	05/15/2001	Monitoring of Gene Expression by Detecting Hybridization to Nucleic Acid Arrays Using Anti-Heteronucleic Acid Antibodies
6,271,002	08/07/2001	RNA Amplification Method
6,300,078	10/09/2001	Computer System & Method for Determining Number of Primary Targets of a Drug
6,303,291	10/16/2001	Methods for Comparing Modes of Action of Two or More Drug Compositions
6,324,479	11/27/2001	Methods of Determining Protein Activity Levels Using Gene Expression Profiles
6,351,712	02/26/2002	Statistical Combining of Cell Expression Profiles
6,352,853	03/05/2002	Multichannel Electrode Arrays
6,370,478	04/09/2002	Methods for Drug Interaction Prediction Using Biological Response Profiles
6,453,241	09/17/2002	Method & System for Analyzing Biological Response Signal Data
6,461,807	11/10/2002	Methods for Drug Target Screening
6,468,476	10/22/2002	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns

**SCHEDULE 2 (continued)**

U.S. Patent Applications		
Serial #	Date filed	Title
09/108,104	06/30/1998	Systems & Methods for the Functional Selection of Cloned DNA Inserts
09/213,120	12/15/1998	Mammalian CAAX Processing Enzymes
09/220,142	12/23/1998	Methods of Characterizing Drug Activities Using Consensus Profiles
09/220,274	12/23/1998	Methods for Robust Discrimination of Profiles
09/220,275	12/23/1998	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns
09/222,597	12/28/1998	Methods for Robust Discrimination of Profiles
09/282,243	03/31/1999	Methods for Identifying Pathway-Specific Reporters & Target Genes and Uses Thereof
09/292,657	04/15/1999	Quantitative Methods, Systems & Apparatuses for Gene Expression Analysis
09/364,751	07/30/1999	Iterative Probe Design & Detailed Expression Profiling with Flexible In-Situ Synthesis Arrays
09/374,565	08/13/1999	Methods for Identifying Pathways of Drug Action
09/408,582	09/29/1999	Methods of Ranking Oligonucleotides for Specificity Using Wash Dissociation Histories
09/454,889	12/03/1999	Targeted Methods of Drug Screening Using Co-Culture Methods
09/469,360	12/22/1999	Method & System for Analyzing Biological Response Data
09/539,697	03/31/2000	Essential Genes of Yeast as Targets for Antifungal Agents, Herbicides, Insecticides & Anti-Proliferation Drugs
09/540,806	03/31/2000	Methods for the Identification of Reporter & Target Molecules Using Comprehensive Gene Expression Profiles
09/561,487	04/28/2000	Iterative Probe Design & Detailed Expression Profiling with Flexible In-Situ Synthesis Arrays
09/616,849	07/14/2000	Method for Determining the Specificity & Sensitivity of Oligonucleotides for Hybridization
09/724,538	11/28/2000	Compositions & Methods for Exon Profiling
09/779,004	02/07/2001	Functionating Genomes with Cross Species Co-Regulation
09/781,814	02/12/2001	Gene Discoveries Using Microarrays

**SCHEDULE 2 (continued)**

<b>U.S. Patent Applications</b>		
<b>Serial #</b>	<b>Date filed</b>	<b>Title</b>
09/783,474	02/14/2001	Methods of Monitoring Disease States and Therapies Using Gene Expression Profiles
09/823,322	04/02/2001	Methods of Determining Therapeutic Index from Gene Expression Profiles
09/898,559	07/02/2001	Methods for Generating Differential Profiles by Combining Data Obtained in Separate Measurements
09/946,290	09/04/2001	Methods for Identifying Pathway-Specific Reporters and Target Genes & Uses Thereof
09/952,334	09/13/2001	Mammalian CAAX Processing Enzymes
09/965,602	09/27/2001	Essential Genes of Yeast as Targets for Antifungal Agents, Herbicides, Insecticides & Anti-Proliferation Drugs
09/975,843	10/12/2001	Methods of Determining Protein Activity Levels Using Gene Expression Profiles
10/001,282	11/30/2001	Use of Profiling for Detecting Aneuploidy
10/058,696	01/28/2002	Statistical Combining of Cell Expression Profiles
10/092,285	03/05/2002	Microarray Reaction Cartridge
10/171,581	06/14/2002	Signature Genes in Chronic Myelogenous Leukemia
10/172,118	06/14/2002	Diagnosis & Prognosis of Breast Cancer Patients
10/182,209	07/22/2002	Barcode Synthetic Lethal Screening to Identify Drug Targets
10/186,383	06/28/2002	Method & System for Analyzing Biological Response Signal Data
10/201,481	07/19/2002	Genes & Proteins Associated with T-cell Activation
10/205,841	07/26/2002	Methods for Identification of Reporter & Target Molecules Using Comprehensive Gene Expression Profiles
10/273,489	10/19/2002	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Profiles
10/287,130	11/04/2002	Statistical Combining of Cell Expression Profiles
60/127,223	03/31/1999	Methods for the Identification of Reporter & Target Molecules Using Comprehensive Gene Expression Profiles

**SCHEDULE 2 (continued)**

U.S. Patent Applications		
Serial #	Date filed	Title
60/127,272	03/31/1999	Essential Genes of Yeast as Targets for Antifungal Agents, Herbicides, Insecticides and Anti-Proliferation Drugs
60/138,620	06/11/1999	Telomere-Specific Pathway Reporter & Target Gene, and Uses Thereof
60/144,382	07/16/1999	Iterative Probe Design & Detailed Expression Profiling with Flexible In-Situ Synthesis Arrays
60/154,563	09/17/1999	Methods for Determining the Specificity & Sensitivity of Oligonucleotides for Hybridization
60/177,460	01/20/2000	Barcode Synthetic Lethal Screening to Identify Drug Targets
60/215,935	07/05/2000	Methods for Genetic Interpretation & Prediction of Phenotype
60/215,936	07/05/2000	Methods & Compositions for Determining Gene Function
60/227,902	08/25/2000	Compositions & Methods for Exon Profiling
60/227,966	08/25/2000	Gene Discovery Using Microarrays
60/250,597	12/01/2000	Use of Profiling for Detecting Aneuploidy
60/253,641	11/28/2000	Random-Primed Reverse Transcriptase In-Vitro Transcription Method for RNA Amplification
60/268,173	02/12/2001	Confirming the Exon Content of RNA Transcripts by PCR Using Primers Complementary to Each Respective Exon
60/286,588	04/26/2001	Methods & Compositions for Utilizing Changes of Hybridization Signals During Approach to Equilibrium
60/296,495	06/06/2001	Hybridization Cartridge for Microarrays
60/298,914	06/18/2001	Signature Genes of Chronic Myelogenous Leukemia
60/298,918	06/18/2001	Prognosis of Breast Cancer Patients
60/306,968	07/20/2001	Genes & Proteins Associated with T-cell Activation
60/309,067	07/31/2001	Methods & Compositions for Utilizing Changes of Hybridization Signals During Approach to Equilibrium
60/316,648	08/31/2001	Methods for Preparing Nucleic Acid Samples Useful for Screening DNA Arrays
60/353,416	02/01/2002	Computer System & Method for Identifying Genes and Determining Pathways Associated with Traits

**SCHEDULE 2 (continued)**

U.S. Patent Applications		
Serial #	Date filed	Title
60/353,845	01/31/2002	Methods for Analysis of Measurement Errors in Measured Signals
60/377,714	05/03/2002	LXR-Ligand Induced Genes & Proteins
60/380,710	05/14/2002	Diagnosis & Prognosis of Breast Cancer Patients
60/381,437	05/16/2002	Computer System & Method for Identifying Genes and Determining Pathways Associated with Traits
60/382,036	05/20/2002	Computer System & Methods for Subdividing a Complex Disease into Component Diseases
60/382,629	06/28/2002	Methods to Assess Quality of Microarrays
60/385188	05/30/2002	Splice Variant Isoform of Human HMG Co-A Reductase
60/400,003	07/30/2002	Novel Splice Variant Isoforms of Human Calcium Channel
60/400,522	08/02/2002	Computer Systems & Methods that Use Clinical & Expression Quantitative Trait Loci to Associate Genes with Traits
60/407,155	08/29/2002	Splice Variant Isoforms of Human HMG Co-A Reductase
60/408,058	09/03/2002	Splice Variant Isoform of Human PHKA2
60/409,094	09/09/2002	Splice Variant Isoform of Human GRM2
60/421,220	10/25/2002	Splice Variant Isoforms of Human Calcium Channel CACNA1B

**SCHEDULE 2 (continued)**

<b>National Patent Applications</b>		
<b>Serial #</b>	<b>Country</b>	<b>Title</b>
22080/00	Australia	Method & System for Analyzing Biological Response Signal Data
23855/00	Australia	Statistical Combining of Cell Expression Profiles
37899/99	Australia	Methods of Determining Protein Activity Levels Using Gene Expression Profiles
38906/99	Australia	Identifying Pathways of Drug Action
14517/00	Australia	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns
40751/99	Australia	Quantitative Methods, Systems & Apparatuses for Gene Expression Analysis
46936/99	Australia	Methods of Monitoring Disease States & Therapies Using Gene Expression Profiles
61595/99	Australia	Methods for Identifying Multiple Primary Targets of a Drug
49635/99	Australia	Methods for Testing Biological Network Models

**SCHEDULE 2 (continued)**

National Patent Applications		
Serial #	Country	Title
2,331,510	Canada	Quantitative Methods, Systems & Apparatuses for Gene Expression Analysis
2,331,621	Canada	Identifying Pathways of Drug Action
2,331,754	Canada	Methods of Determining Protein Activity Levels Using Gene Expression Profiles
2,335,187	Canada	Methods for Testing Biological Network Models
2,335,299	Canada	Methods of Monitoring Disease States & Therapies Using Gene Expression Profiles
2,344,267	Canada	Methods for Identifying Multiple Primary Targets of a Drug
2,348,837	Canada	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns
2,356,648	Canada	Methods of Characterizing Drug Activities Using Consensus Profiles
2,356,655	Canada	Method & System for Analyzing Biological Response Signal Data
2,356,673	Canada	Methods for Drug Interaction Prediction Using Biological Response Profiles
2,356,696	Canada	Statistical Combining of Cell Expression Profiles
2,356,873	Canada	Methods for Determining Therapeutic Index from Gene Expression Profiles
2,356,891	Canada	Methods for Robust Discrimination of Profiles
2,378,933	Canada	Iterative Probe Design & Detailed Expression Profiling with Flexible In-Situ Synthesis Arrays
2,379,212	Canada	Method for Determining Specificity & Sensitivity of Oligonucleotides for Hybridization
2,393,360	Canada	Targeted Methods of Drug Screening Using Co-Culture Methods
2,398,690	Canada	Bar-Coded Synthetic Lethal Screening to Identify Drug Targets

**SCHEDULE 2 (continued)**

National Patent Applications		
Serial #	Country	Title
00948665.5	EPC	Iterative Probe Design & Detailed Expression Profiling with Flexible In-Situ Synthesis Arrays
00948666.3	EPC	Method for Determining Specificity & Sensitivity of Oligonucleotides for Hybridization
00982313.9	EPC	Targeted Methods of Drug Screening Using Co-Culture Methods
01942675.8	EPC	Bar-Coded Synthetic Lethal Screening to Identify Drug Targets
99920392.0	EPC	Methods of Determining Protein Activity Levels Using Gene Expression Profiles
99921786.2	EPC	Identifying Pathways of Drug Action
99924189.6	EPC	Quantitative Methods, Systems & Apparatuses for Gene Expression Analysis
99930384.5	EPC	Methods for Testing Biological Network Models
99930385.2	EPC	Methods of Monitoring Disease States & Therapies Using Gene Expression Profiles
99948412.4	EPC	Methods for Identifying Multiple Primary Targets of a Drug
99966569.8	EPC	Method & System for Analyzing Biological Response Signal Data
99966667.0	EPC	Methods for Determining Therapeutic Index from Gen Expression Profiles
99967502.8	EPC	Methods of Characterizing Drug Activities Using Consensus Profiles
99967594.5	EPC	Statistical Combining of Cell Expression Profiles
99967595.2	EPC	Methods for Drug Interaction Prediction Using Biological Response Profiles
99968165.3	EPC	Methods for Robust Discrimination of Profiles
99971047.8	EPC	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns

**SCHEDULE 2 (continued)**

National Patent Applications		
Serial #	Country	Title
12-548499	Japan	Identifying Pathways of Drug Action
12-548511	Japan	Quantitative Methods, Systems & Apparatuses for Gene Expression Analysis
12-548781	Japan	Methods of Determining Protein Activity Levels Using Gene Expression Profiles
12-554833	Japan	Methods of Monitoring Disease States & Therapies Using Gene Expression Profiles
12-554875	Japan	Methods for Testing Biological Network Models
12-574301	Japan	Methods for Identifying Multiple Primary Targets of a Drug
12-578488	Japan	Methods for Using Co-Regulated Genesets to Enhance Detection & Classification of Gene Expression Patterns
12-591224	Japan	Methods of Characterizing Drug Activities Using Consensus Profiles
12-591225	Japan	Methods for Robust Discrimination of Profiles
12-591226	Japan	Method & System for Analyzing Biological Response Signal Data
12-591227	Japan	Statistical Combining of Cell Expression Profiles
12-591228	Japan	Methods for Drug Interaction Prediction Using Biological Response Profiles
12-591229	Japan	Methods for Determining Therapeutic Index from Gen Expression Profiles
13-511150	Japan	Iterative Probe Design & Detailed Expression Profiling with Flexible In-Situ Synthesis Arrays
13-511221	Japan	Method for Determining Specificity & Sensitivity of Oligonucleotides for Hybridization
13-542581	Japan	Targeted Methods of Drug Screening Using Co-Culture Methods
13-553391	Japan	Bar-Coded Synthetic Lethal Screening to Identify Drug Targets

**SCHEDULE 2 (continued)**

<b>Activ PCT Patent Applications</b>		
<b>Serial #</b>	<b>Country</b>	<b>Title</b>
PCT/US00/35352	PCT	Use of Profiling for Detecting Aneuploidy
PCT/US01/20928	PCT	Methods & Compositions for Determining Gene Function
PCT/US01/20931	PCT	Methods for Genetic Interpretation & Prediction of Phenotype
PCT/US01/26274	PCT	Gene Discovery Using Microarrays
PCT/US01/26541	PCT	Compositions & Methods for Exon Profiling
PCT/US01/44821	PCT	Random-Primed Reverse Transcriptase In-Vitro Transcription Method for RNA Amplification
PCT/US01/48527	PCT	Sample Tracking Using Molecular Barcodes
PCT/US02/04219	PCT	Confirming Exon Content of RNA Transcripts by PCR Using Primers Complementary to Each Respective Exon
PCT/US02/12757	PCT	Methods & Compositions for Utilizing Changes of Hybridization Signals During Approach to Equilibrium
PCT/US02/18947	PCT	Diagnosis & Prognosis of Breast Cancer Patients
PCT/US02/20835	PCT	Methods of Generating Differential Profiles by Combining Data Obtained in Separate Measurements
PCT/US02/22787	PCT	Methods for Preparing Nucleic Acid Samples Useful for Screening DNA Arrays